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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,620	10/25/2001	Abraham Scaria	5046US	2242
7590 04/04/2006				
Genzyme Corporation 15 Pleasant Street Connector P.O. Box 9322 Framingham, MA 01701-9322			EXAMINER WEHBE, ANNE MARIE SABRINA	
			ART UNIT 1633	PAPER NUMBER
DATE MAILED: 04/04/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/057,620

Applicant(s)

SCARIA ET AL.

Examiner

Anne Marie S. Wehbe

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 December 2005.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 1-52 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 5-16, 23-34 and 38-49 is/are allowed.
- 6) ☒ Claim(s) 1-4, 17-22, 35-37, 50 and 51 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Applicant's response received on 12/30/05 has been entered. No claims have been amended, canceled, or added. Claims 1-52 are pending and currently under examination.

#### ***Claim Rejections - 35 USC § 112***

The rejection of claims 2, 4, 17-18, 20, 22, 35, 37, 50, and 52 under 35 U.S.C. 112, first paragraph, for lack of enablement is withdrawn over claims 2, 4, 18, 20, 22, 37, and 52 and maintained in part over claims 17, 35, and 50. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the remaining grounds of rejection for reasons of record as discussed in detail below.

Applicant's argument that the specification on page 26 incorporates by reference the teachings of Seidah et al., which includes the SKI-1 consensus sequence, is persuasive in overcoming the lack of guidance in the specification for an SKI-1 consensus sequence capable of being cleaved by SKI-1.

In regards to the putative SKI-1 sequence of SEQ ID NO:9, the applicant argues that the skilled artisan would have no reason to doubt that this sequence wouldn't be cleaved by SKI-1. This is not agreed. The previous office action provided just such as reason which is reiterated for applicant's convenience below.

As stated in the previous office action, while the specification discloses that the Factor VII nucleic acid sequence can be modified such that it is capable of expressing a modified Factor

Art Unit: 1633

VII polypeptide which contains an SKI-1 cleavage site located in the area of amino acid 147-154 of the wild type Factor VII amino acid sequence, and preferably wherein amino acids 151-154 of human Factor VII have been replaced with the amino acid sequence of SEQ ID NO:9, the specification fails to provide an enabling disclosure that replacement of amino acids 151-154 of the wild type human Factor VII amino acid sequence with the amino acid sequence of SEQ ID NO:9 would in fact result in a modified Factor VII polypeptide capable of being cleaved by SKI-1. In regards to the specific replacement of amino acids 151-154 with SEQ ID NO:9, it is first noted that Figure 3 in fact shows the replacement of amino acids 147-154, not amino acids 151-154 with the amino acids of SEQ ID NO:9. Further, the working examples provide only a brief prophetic description on page 26 of modifying the amino acid sequence of Factor VII around amino acid 152 to include an SKI-1 cleavage site as encoded by SEQ ID NO:9. The specification does not provide any actual results which demonstrate that SEQ ID NO:9 is a cleavable by SKI-1. Further, as discussed in the previous office action, at the time of filing, SKI-1, which stands for subtilisin/kexin isozyme-1, was a novel proprotein convertase. The literature published prior to the effective filing date of this application teaches that SKI-1 has a unique cleavage specificity from other proprotein convertases. Seidah et al. teaches that at the time of filing, the cleavage site for SKI-1 cleavage was determined to be (R/K) -X-X-(L/T)↓ (Seidah et al. (1999) Brain Research, Vol. 848, 45-62). Although it is acknowledged that the specification references Seidah et al., the specification teaches a different consensus sequence (R/K) -X -(R/K)-(L/V/F) -Z (SEQ ID NO:20), which is found in SEQ ID NO:9 as claimed (see Figure 3). Thus the alternate consensus cleavage sequence for SKI-1 identified in SEQ ID NO:9 does not correspond to that disclosed and demonstrated to be effective in the literature at the time of filing. Therefore, in

Art Unit: 1633

view of the teachings of Seidah et al. that the SKI-1 cleavage is (R/K) -X-X-(L/T)<sub>↓</sub>, the skilled artisan would not have been able to predict *a priori* that a sequence which does not contain this consensus cleavage site would be capable of being cleaved by SKI-1. As such, in view of published consensus cleavage sequence for SKI-1, the breadth of the claims, and the lack of working examples which demonstrate that alternate cleavage consensus sequences for SKI-1 cleavage exist and in particular that SEQ ID NO:9 is capable of being cleaved by SKI-1, it would have required undue experimentation to practice the invention as claimed.

### ***Claim Rejections - 35 USC § 102***

The rejection of claims 1, 3, 18-19, 21, 36, and 51 under 35 U.S.C. 102(e) as being anticipated by WO 01/70763 A1 (2001), hereafter referred to as High et al., which designated the United States and was published in English, and which claims priority to US provisional application 60/191,331, filed 3/22/00, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant rejection of the claims for reasons of record as discussed in detail below.

The applicant argues that High et al. cannot anticipate the instant claims because High cannot rely on the priority date of provisional application 60/191,331 because the specification of 60/191,331 does not teach or suggest mutating the endogenous cleavage site of Factor VII to encode for the cleavage site of furin. The applicant states that the specification of 60/191,331 differs from the specification of WO 01/70763 A1 by only teaching insertion of additional amino acids that code for the furin cleavage site. The applicant states that the provisional

application is missing the teachings in the WO 01/70763 A1 document for mutation of the endogenous sequence and that therefore WO 01/70763 A1 cannot anticipate the instant claims under 35 U.S.C. 102(e).

In response, review of the provisional application 60/191,331 does support applicant's argument that the provisional only teaches insertion of a cleavage site between amino acids 152 and 153 of Factor VII. However, the previous office action clearly stated that the claims as written are broad and encompass **both** the insertion of a furin cleavage sequence between amino acids 152-153 or the substitution of a furin cleavage sequence for the native cleavage site. Specifically, the previous action pointed out that the mutation of one or more amino acids within amino acids 147-154 of Factor VII can include simple substitution of one amino acid residue for another or the insertion of additional amino acids to this area. The rejection of record further points out that the claims clearly read on mutations including the addition of amino acids, see claims 5, 26, and 41 which recite that amino acids 147-154 are replaced by the amino acid sequence of SEQ ID NO:5 where SEQ ID NO:5 adds an additional amino acid to the length of the protein. The provisional application, as acknowledged by applicants, does provide support for the insertion of the furin cleavage site between amino acids 152-153, which is in the area of about amino acid 147 to about amino acid 154 as required by the claims. Thus, the teachings of High, including the provisional application, anticipate this embodiment of the claims as written. It is further noted that the claims as written are not so limited to exclude the embodiment wherein an extra peptide is released in addition to the Factor VII heavy and light chain molecules upon cleavage with furin. Thus, based on the breadth of the claims as written, which do not place any limitations on the kind of mutation made to the endogenous cleavage site and which do not

Art Unit: 1633

exclude additional products resulting from cleavage with furin besides the heavy and light chain of Factor VII, applicant's arguments are not found persuasive.

Thus, for the reasons set forth above, the rejection of record stands.

### ***Claim Rejections - 35 USC § 103***

The rejection of claims 2, 4, 20, 22, 37, and 52 under 35 U.S.C. 103(a) as being unpatentable over WO 01/70763 A1 (2001), hereafter referred to as High et al., which designated the United States and was published in English, and which claims priority to US provisional application 60/191,331, filed 3/22/00, in view of Seidah et al. (1999) Brain Research, Vol. 848, 45-62, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed below.

The applicant argues that WO 01/70763 A1, High et al., does not qualify as prior art under 35 U.S.C. 102(e) over the claims because the provisional application to which the WO document claims benefit does not disclose substituting the furin cleavage site for the endogenous site. This argument has been addressed in detail in the above response to the rejection of the claims under 35 U.S.C. 102(e) and has not been found persuasive, see above.

The applicant has not provided any additional arguments traversing the instant grounds of rejection. Therefore, the rejection of record stands.

### ***Allowable Subject Matter***

Claims 5-16, 23-34, and 38-49 continue to be objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

***Information Disclosure Statement***

The information disclosure statement filed 12/30/05 has been considered and an initialed copy of the IDS is attached to this office action.

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.



Art Unit: 1633

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Dave Nguyen, can be reached at (571) 272-0731. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

ANNE M. WEHBE PH.D.  
PRIMARY EXAMINER  
